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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,122	06/25/2001	Shohei Tanaka	Q64929	2326

7590 07/17/2002  
Sughrue Mion Zinn Macpeak & Seas  
2100 Pennsylvania Avenue NW  
Washington, DC 20037

EXAMINER
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HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 07/17/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/869,122

Applicant(s)

TANAKA ET AL.

Examiner

San-ming Hui

Art Unit

1617

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 June 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 1 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: None.

Claim(s) objected to: None.

Claim(s) rejected: 7 and 9-13.

Claim(s) withdrawn from consideration: None.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11.
10. ☐ Other: \_\_\_\_\_

RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200

### DETAILED ACTION

Continuation of 5):

Applicant's remarks filed June 27, 2002 regarding bisphosphonate's direct anti-tumor activities leads to Shipman's conclusion of increased survival rate by bisphosphonate have been considered but are not found persuasive. Direct anti-tumor activity of bisphosphonate is only one of the many reasons that may explain why the survival rates are increased in the clinical trials of bisphosphonate for treatment of multiple myeloma. In Shipman et al. page 132, col. 2 – page 133, col. 1, three potential reasons are given to explain the increased survival rate in multiple myeloma patients treated with bisphosphonate and direct anti-tumor activity observed with bisphosphonate treatment is only one of them.

Applicant's remarks on the newly cited references have been considered but are not found<sup>\*</sup> persuasive. The authors of Shipman et al. have considered all the newly cited references, and numerous other references related to multiple myeloma treatment with bisphosphonate. Furthermore, after Shipman et al. considered all these published references, as a whole, they concluded that "it remains possible that bisphosphonates may not only be effective in the treatment of bone disease associated with multiple myeloma, but may also have a direct anti-tumor effect upon myeloma cells." On page 136, col. 1. Shipman et al. was published in a peer-review journal. If the applicant feels strongly that the teachings of the references cited in Shipman et al. would not lead to the conclusion made in the article, applicant is encouraged to present published

information refuting Shipman et al. Examiner would favorably consider a declaration by Dr. Shipman admitting that the conclusion in his article is not factually based, or in error.

Applicant's remarks regarding the dosage of the instant compound have been considered and are not found persuasive. Isomura et al. teaches the oral daily dose is 1 mg to 1g/adult, which is encompassed the dosage range recited the instant claims. The optimization of result therapeutic parameters (e.g., dosage range) is obvious as being within the skill of the artisan, absent evidence to the contrary.

Applicant's remarks regarding the data of the examples averring a lower dosage of the instant compound as compared to that of the other agents would illustrate unexpected results have been considered, but are not found persuasive. Lower dosage of one agent as compared to other agents does not necessarily means that the agents will be more effective than the other agents. It merely means that the agent, which required less dosage to achieve the same pharmacological effect, is more potent than the agents that need larger dosage. And it does not have any implication on the side effect profile of the agent. The results from the examples of the instant specification are seen as the expected results over the cited prior art. Therefore, no clear and convincing unexpected results are seen herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

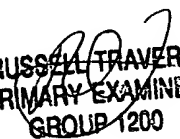
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui  
July 15, 2002

  
RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200